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Differential Durability of Immune Responses to Measles and Mumps Following MMR Vaccination

Richard B. Kennedy[1,*], **Inna G. Ovsyannikova**[1], **Antonia Thomas**[2], **Beth R. Larrabee**[3], **Steven Rubin**[2], and **Gregory A. Poland**[1]

[1]Mayo Clinic Vaccine Research Group, U.S. Department of Health and Human Services, Silver Spring, MD 20993

[2]Center for Biologics Evaluation and Research, Food and Drug Administration, U.S. Department of Health and Human Services, Silver Spring, MD 20993

[3]Division of Biomedical Statistics and Informatics, Department of Health Science Research, Mayo Clinic, Rochester, MN 55905 USA

Abstract

The development and wide-spread use of mumps vaccine resulted in a dramatic and sustained decrease in the incidence of mumps disease; however, since 2000, an increase in the size and number of mumps outbreaks in the United States and other countries has sparked renewed interest in the durability of mumps-specific immunity elicited by mumps vaccination. The most likely explanation for mumps cases in previously immunized persons may be secondary vaccine failure, or waning immunity. In the current study, we examined changes in markers of measles and mumps immunity at two timepoints, approximately 7 and 17 years after two-dose MMR-II® vaccination, in a cohort of 98 healthy adults.

[*]Address correspondence to: Richard B. Kennedy, Ph.D., Co-Director, Mayo Vaccine Research Group, Mayo Clinic, Guggenheim 611D, 200 First Street SW, Rochester, Minnesota 55905, Phone: (507) 284-4968; Fax: (507) 266-4716; kennedy.rick@mayo.edu.

Disclosures

Dr. Poland is the chair of a Safety Evaluation Committee for novel investigational vaccine trials being conducted by Merck Research Laboratories. Dr. Poland offers consultative advice on vaccine development to Merck & Co. Inc., Avianax, Adjuvance, Valneva, Medicago, Sanofi Pasteur, GlaxoSmithKline, and Emergent Biosolutions. Dr. Poland's effort on this project was covered by the abovementioned NIH grants. Dr. Poland did not receive any support from the Merck Investigator Studies Program grant. Drs. Poland and Ovsyannikova hold patents related to measles and vaccinia peptide research. Dr. Kennedy holds a patent related to vaccinia peptide research. Dr. Kennedy has received funding from the Merck Investigator Studies Program to study waning immunity to mumps vaccine. These activities have been reviewed by the Mayo Clinic Conflict of Interest Review Board and are conducted in compliance with Mayo Clinic Conflict of Interest policies.

Dr. Poland is the chair of a Safety Evaluation Committee for novel non-rubella investigational vaccine trials being conducted by Merck Research Laboratories. Dr. Poland offers consultative advice on vaccine development to Merck & Co. Inc., Avianax, Adjuvance, Valneva, Medicago, Sanofi Pasteur, GlaxoSmithKline, and Emergent Biosolutions. Drs. Poland and Ovsyannikova hold three patents on measles and vaccinia peptide research. Dr. Kennedy holds a patent on vaccinia peptide research. Dr. Kennedy has also received funding from Merck Research Laboratories to study waning immunity to mumps. All other authors declare no competing financial interests. These activities have been reviewed by the Mayo Clinic Conflict of Interest Review Board and are conducted in compliance with Mayo Clinic Conflict of Interest policies. This research has been reviewed by the Mayo Clinic Conflict of Interest Review Board and was conducted in compliance with Mayo Clinic Conflict of Interest policies.

Our results indicate that mumps IgG titers exhibited a large and significant decline during this time period, while mumps neutralizing Ab titers were relatively stable. There was a similar discrepancy with measles-specific immune responses. For both pathogens, neutralizing antibody titers were fairly low and, given the length of time since vaccination, may have already declined. These data suggest that specific immune outcomes may wane at different rates and highlight our currently incomplete understanding of protective immune responses to mumps and measles.

Keywords

Mumps; Mumps Vaccine; Mumps virus; Measles; Measles Vaccine; Measles Virus; MMR-II Vaccine; Antibodies; Humoral Immunity; T cell ELISPOT; Cell-mediated Immunity

Introduction

Mumps is one of the earliest documented human diseases and was first described by physicians in ancient Greece [1]. The most common symptom is salivary gland swelling, although orchitis, mastitis and, more rarely, encephalitis, meningitis, myocarditis, and deafness have also been reported [2]. Subclinical infections are also thought to be relatively common and may boost immunity [3]. Mumps is caused by an enveloped negative strand RNA paramyxovirus. IgM antibody is detectable soon after infection; viral neutralizing IgG peaks 1-3 months after vaccination, then declines over a period of several months [4]. Antibody (Ab) responses remain detectable for decades after infection. Vaccination also elicits long-lived humoral responses, albeit at lower titers than natural infection [5]. Multiple studies have demonstrated that mumps Ab responses, including neutralizing Ab titers, decline significantly over time [6–9]. Neutralizing Ab is associated with protection, but no specific titer has been identified as a correlate of protection [10]. While ELISAs are commonly used to assess mumps immunity, they detect both neutralizing and non-neutralizing Ab; thus, there is less confidence in the assay's ability to assess functional antibody and protection. Indeed, several studies have found an unsatisfactory correlation between ELISAs and functional assays that measure virus neutralizing activity [11–15]. In some cases, this lack of correlation is due to the presence of cross-reacting antibodies against parainfluenza viruses, which can be detected in mumps virus ELISAs [11, 16, 17]. Cellular immunity also develops following infection or vaccination, with antigen-specific T cells appearing within 1 month of infection and persisting for years. Humoral and cellular responses are not highly correlated with one another, and the extent to which cellular immunity contributes to protection against infection, long-term protection against disease, and/or clearance of disease is not well understood.

Mumps virus was first identified by Johnson and Goodpasture in 1935 [18]. After the advent of *in vitro* culture systems in the mid 1940s, the first inactivated mumps vaccines were developed [19, 20]. These vaccines produced short-lived immunity and were superseded by live attenuated strains. In the United States, the use of a live attenuated mumps vaccine (Jeryl Lynn strain) began in 1967 [21]. Since 1971, mumps vaccine has been given as a combination vaccine (MMR) that includes measles and rubella viruses. In 1989, the United

States instituted a 2-dose MMR-II vaccination policy, with a first dose recommended at 12-18 months of age and a second dose at 4-6 years of age.

Widespread use of the two-dose MMR immunization schedule dramatically decreased the occurrence of mumps in the United States, but has not eliminated it; regular outbreaks involving hundreds to several thousand cases occur every year [10]. Despite the very high vaccination rates, the highest incidence rate for these outbreaks is among people in their late teens and early twenties, mostly on college and university campuses or sport teams. The likely cause for these outbreaks is waning immunity, as strong evidence shows correlation between time since vaccination and 1) declining Ab titers, 2) decreased vaccine efficacy, and 3) increased risk of infection [22].

Here we report findings from a cohort of 98 MMR-II vaccine recipients whose immune responses to mumps and measles were assessed at two timepoints, approximately 7 and 17 years post-vaccination. Our primary objective was to evaluate whether or not immune responses to either virus waned over this time frame.

Methods

Human Subjects

Participants were selected from a cohort of 1,025 school-aged children (11-22 years of age) recruited for a rubella vaccine response study. These subjects were recruited from Olmsted County, MN, USA, between 2001 and 2009 [23]. Each of these subjects had two documented doses of MMR-II® vaccine. A blood draw was obtained at the time of the rubella vaccine study, which was ~7 years after receipt of the second dose of MMR-II® vaccine. Individuals still living in the local area were invited to participate in a second blood draw which was taken about ~17 years after the second MMR-II® vaccination. Individuals still living in the local area were invited to participate in an additional blood draw which was taken about ~17 years after the second MMR-II® vaccination. Informed consent was obtained from 98 subject,s and all study procedures were approved by the Mayo Clinic Institutional Review Board. Established protocols were used to isolate and cryopreserve serum and peripheral blood mononuclear cells (PBMCs) from each subject [24].

Humoral Immune Response Assays

Mumps and measles serum IgG titers were assessed using a commercial ELISA (Zeus Scientific; Branchburg NJ). Measles virus-specific neutralizing Ab titers were measured using a previously described high-throughput fluorescence-based plaque reduction microneutralization (PRMN) assay developed in our laboratory for population-based immunogenetic studies, with assay variability, as measured by its coefficient of variation (CV) of 5% [25]. Measles virus Edmonston strain was used for this assay. Mumps virus-specific neutralizing Ab titers were measured in an FDA laboratory using a standardized plaque-reduction neutralization assay using the Jeryl Lynn strain of mumps as previously described [26]. A robustness study determined that the assay CV was 16%.

IFNγ T Cell ELISPOT Assays

Cellular immune responses were characterized through the use of an IFNγ ELISPOT assay. Specifically, 200,000 PBMCs were added to each well of a 96-well ELISPOT plate along with measles virus (Edmonston strain, multiplicity of infection [MOI]=0.5) or mumps virus (Jeryl Lynn strain, MOI=0.5) for 24 hours. Unstimulated wells served as negative controls, with phytohemagluttinin (PHA)-stimulated cells serving as a positive control. ELISPOT plates were developed as per manufacturer's protocols (B.D. Biosciences; San Diego, CA) and spots were quantitated using an automated ELISPOT reader (C.T.L.; Shaker Heights, OH).

Statistical Analysis

Select demographics were summarized using medians and inter-quartile ranges for continuous variables and percentages for categorical variables. Tests for a median change in neutralizing Ab titers from first blood draw to second blood draw were conducted using Wilcoxon-Signed Rank tests for both mumps and measles. Neutralizing Ab titer was then subjected to a log transformation for use in linear models. These linear models were employed so that we may investigate the effect of potential confounders on the association of time with humoral response. Indicator variables for seroprotection at each blood draw were created and utilized in McNemar's tests. Spearman correlations were used to investigate the association of humoral immunity between the pathogens at each timepoint.

Cellular immune responses were summarized as the difference between the mean stimulated and mean unstimulated IFNγ ELISPOT responses. These differences were then probit transformed for use in linear mixed models with person defining the random component. Potentially important covariates were evaluated univariately, and then with backwards selection, with this transformed outcome. Covariates selected for use in the final models for measles response were PHA, date of most recent recorded vaccination, and the time since last vaccination. For mumps, the covariates were PHA and date of most recent vaccination. Retained covariates were forced into a model to evaluate the importance of gender in relation to cellular response. Time since last vaccination was then considered in models with retained covariates and gender. For each of the waning immunity comparisons, subjects with missing data or non-existent biospecimens at one or both timepoints were excluded from analysis.

Results

Study Subjects

Each of the 98 individuals participating in this study had received 2 documented doses of MMR-II. Past participants with existing sera samples and PBMC samples still residing in southeast Minnesota were enrolled in the study and underwent an additional blood draw. The demographics (e.g., age, gender, time since last vaccination, time between blood draws) for the mumps-specific and measles-specific analyses are provided in Table 1.

Markers of Mumps-specific Humoral Immunity

Mumps IgG titers were found to drop significantly between the two timepoints (Figure 1A). Median IgG titers dropped two-fold (optical density, OD: 0.3 to 0.15) in the time between the blood draws. Mumps-specific neutralizing Ab titers for each subject were also evaluated (Figures 1C and 2A). In marked contrast to the total IgG titers, we did not detect a significant decrease in neutralizing Ab titer with increasing time since the first blood draw (which ranged from 5.2 to 8.7 years after receipt of the second MMR dose). The histograms in Figure 3 depict the mumps-specific Ab titers for each blood draw. The median titer at the first blood draw was 74.8, with an interquartile range of 35.1 – 170.2. The median titer at the second blood draw (which was between 7.6 and 14.2 years after the first blood draw) was 69.8, with an interquartile range of 25.1 – 146.2. The difference in Ab titers between the two blood draws (Figure 3C) was not statistically significant (p=0.17). The time between blood draws did not exhibit a statistically significant association (p=0.82) with the difference in titer. Without a defined correlate of protection, we cannot identify those whose seroprotected status changed between timepoints; therefore, we utilized an arbitrary threshold (>20% drop in neutralizing Ab titer across the two timepoints) and found that 35 subjects, just over a third of the cohort, had such a drop in neutralizing Ab titer over time.

Markers of Measles-specific Humoral Immunity

Measles serum IgG titers also exhibited clear evidence of a decrease over time: they declined by nearly 60% (median OD reading dropped from 0.65 to 0.27) between the two blood draws (Figure 1B). In contrast, when measles-specific neutralizing Ab titers were plotted against time since vaccination, as shown in Figures 1D and 2B, there is only a slight downward trend that was not statistically significant. The median titer at the first blood draw was 604 mIU/mL, with an interquartile range of 348 – 984 mIU/mL. The median titer at the second blood draw was 498, with an interquartile range of 258 – 975 mIU/mL. The difference in Ab titers between blood draws (Figure 4C) was not significant (p=0.15). The time between blood draws did not exhibit a statistically significant association (p=0.36) with the difference in titer. At the individual level, 41 of the subjects experienced a drop in titer of >20%. Using a measles neutralizing Ab titer of 120 mIU/mL as a correlate of protectiont blood draw, 88 subjects (97.8%) were seroprotected at the first blood draw, dropping to 83 subjects (92.2%) at the second blood draw. This difference did not reach statistical significance (p=0.07), likely secondary to limited statistical power.

Markers of Mumps-specific Cellular Immunity

Cellular immune responses to mumps virus were evaluated by IFNγ ELISPOT. PBMC samples from both timepoints were run on the same plate in order to avoid batch effects. At the first timepoint ~ 7 years post-vaccination, the median response was 0.8 IFNγ-producing spots per 200,000 cells (IQR: 0.5 – 1.7). At the second timepoint, ~17 years post-vaccination, the median response was 1.6 IFNγ-producing spots per 200,000 cells (IQR: 0.8 – 3.0). After adjusting for gender, PHA response, and date of second vaccination, the difference between the two timepoints barely met the threshold for significance (p=0.047). As responses were slightly higher at the second timepoint, we did not see evidence of waning immunity; furthermore, it is difficult to assess the clinical or biological significance

of these minor changes in cellular immunity. Our results at each timepoint indicate that IFNγ responses are minimally detectable even seven years after vaccination.

Markers of Measles-specific Cellular Immunity

Cellular immune responses to measles virus were evaluated by IFNγ ELISPOT. As with the mumps ELISPOT, PBMC samples from both timepoints were run on the same plate in order to avoid batch effects. At the first timepoint, the median response was 42.2 IFNγ-producing spots per 200,000 cells (IQR: 18.6 – 78.9). At the second timepoint, the median response was higher: 86 IFNγ-producing spots per 200,000 cells (IQR: 51.1 – 155.0). This difference was adjusted for PHA, gender, and the date of the last know vaccination and remained statistically significant ($p<0.001$).

Effect of Time Since Vaccination on Immune Response

In order to determine whether or not vaccine timing played a role on the immune response to either measles or mumps, we compared subjects with a 20% drop in mumps Ab titer and those without. Our results indicated that there were no significant differences in time between vaccination and first blood draw ($p=0.22$), vaccination and second blood draw ($p=0.15$), or time between first and second blood draw ($p=0.58$) between these two groups of subjects. We repeated this analysis comparing the subjects who became measles seronegative at the second blood draw (first draw titer was >120 mIU/mL and second draw titer was <120 mIU/mL) with those who remained measles seropositive. These results also indicated that there were no significant differences in time between first blood draw and vaccination ($p=0.58$), second blood draw and vaccination ($p=0.99$), or time between first and second blood draws ($p=0.82$) between these two groups.

Effect of Sex on Humoral Immune Response to Mumps and Measles

We examined differences in neutralizing Ab titer between men and women at each timepoint and between timepoints. We did not find statistically significant differences for mumps-specific responses (Figure 5A) or for measles-specific responses (Figure 5B) between males and females at either time point. Nor did we observe significant differences between men and women in the change in Ab titer between timepoints (mumps: $p=0.15$, measles: $p=0.15$).

Discussion

Given the recent increase in mumps cases and outbreaks, it is important to evaluate the duration of vaccine-induced immunity. We examined a limited cohort of 98 two-dose MMR vaccine recipients for evidence of waning immunity to either mumps or measles. We identified a large degree of variability in the magnitude of the immune responses to each viral pathogen. We did not observe any statistically significant correlations between measles and mumps neutralizing Ab titers (Figure 6) or between measles and mumps cellular immune measures. At the population level, our data indicate that different immune outcomes exhibit different degrees of waning immunity during the 7.6- to 14.2-year time period between blood draws. Although total measles and mumps virus-specific IgG levels were lower at the second timepoint, there were no statistically significant differences in measles

or mumps virus-specific neutralizing antibody levels between the two time points, suggesting the absence of waning humoral immunity during this time period..

We did note considerable inter-individual variability in immune responses, with a portion of the cohort exhibiting some degree of waning immunity to one or both pathogens. For example, 35.7% of the cohort experienced a >20% drop in mumps neutralizing Ab titer. Without a defined immune correlate of protection for mumps, it is difficult to estimate the clinical impact of this on the cohort, but there will likely be a few individuals whose immunity dropped below the protective threshold. There are 12 recognized genotypes of mumps virus, though they all belong to the same serotype. Although there is no evidence of immune escape (i.e., all strains can be neutralized by vaccine-elicited Ab) [33], neutralizing activity against each strain can vary greatly; it has been suggested that individuals with low neutralizing Ab titer to the vaccine strain may have inconsistent protection against disease-causing strains [3, 34]. We did not assess this phenomenon in our study.

We also found that 42% of subjects experienced a >20% decrease in measles neutralizing Ab titer. For measles, where we have an established correlate of protection (neutralizing Ab titer of 120 mIU/mL),[27] five subjects dropped below the putative threshold of protection during the time period covered by the study. Although not statistically significant in our cohort, it does represent a drop in herd immunity from 98% to 92%, which is below or at the lower end of the level of herd immunity deemed necessary for measles control (95%-96%). It is also notable that 41 subjects (41.8%) experienced a drop (>20%) in measles Ab titer over the time period studied. When comparing subjects that experienced a drop in Ab titer to subjects whose Ab titers did not drop, we did not see any difference in time between the blood draws and vaccination or the time between each blood draw, suggesting that study-related timing differences among individuals did not account for waning immunity.

When tested in select outbreak settings, administration of a third dose of MMR vaccine has resulted in a transient increase in Ab titer [35–38]. The increase in titer is highly correlated with baseline immunity and returns to close to pre-vaccination levels in about 1 year. This suggests that an individual has a pre-determined immunologic set-point, and any protection provided by a third dose of MMR will be temporary.

Interestingly, for both pathogens, the marker of cellular immunity increased at the later timepoint. The increase in mumps T cell response was statistically significant but quite small (0.8 vs 1.6 spots per 200,000 cells). It is not clear if this difference is biologically relevant. The increase in the measles-specific ELISPOT response was much larger (42 vs 86 spots per 200,000 cells). The increase may be due to a greater variability in the spectrum of response in our cohort, subclinical boosting that preferentially expands antigen-specific T cells, or it could reflect a greater longevity of memory T cells compared to memory B cells. Further investigation of this effect is warranted.

In addition to the subjects who displayed some evidence of declining immune response, we also observed a number of subjects with an increase in immune markers at the later timepoint. In Figure 7, the subjects at the top of the graph exhibited an increase in measles neutralizing Ab titer (but not mumps), while subjects at the far right of the figure

experienced an increase in mumps neutralizing Ab titer (but not measles). Each subject was screened and found negative for a history of disease consistent with measles or mumps infection, and there have not been any outbreaks of measles or mumps in Olmsted County over the lifetime of these study subjects, which suggests the low likelihood of subclinical infection as an explanation for such increases. Careful screening of each subject and a comprehensive review of medical records was also conducted to exclude anyone with more than two documented doses of MMR; nevertheless, it is possible that a few subjects did receive an additional, undocumented dose of vaccine. Undocumented vaccine receipt is a more likely scenario than disease exposure and was our initial hypothesis, but this did not appear to be the case given that those subjects who demonstrated an increase in Ab titer to one pathogen between the two timepoints tested did not exhibit an increase in Ab titer to the other pathogen. Upon further examination, we found that the increase in mumps (or measles) neutralizing Ab titer was not associated with a significant increase in the other mumps-specific (or measles-specific) IgG or IFNγ ELISPOT responses.

Another possible explanation could be the fact that samples from the first blood draw were stored at −80C for several years longer than the samples from the second blood draw; however, there were no statistically significant associations between length of storage and total IgG or neutralizing Ab titer for either pathogen. We have previously reported that multiple freeze-thaw cycles do not negatively impact Ab titers as measured by ELISA [39]. Others have obtained similar results when using ELISAs and have demonstrated that Ab in frozen serum is stable for years [40, 41]. Less information is available on the effect of prolonged frozen storage of serum and PBMCs on functional assays such as virus neutralization assays and ELISPOTs.

One limitation of our study is that we did not have sera or Ab response data from before the second MMR dose or from shortly after second dose vaccination. Nevertheless, we did note that, for the timepoints tested, both humoral and cellular immune measures were significantly lower for mumps than for measles. This finding corresponds with published literature indicating that immune responses to both wild-type and vaccine-strain mumps are weaker than those seen with other viral pathogens [10, 42]. With the obvious caveat that direct comparisons are hampered by differences in assay methodology, our results support the idea that the mumps component of the vaccine is significantly less immunogenic than the measles component, and is characterized by higher rates of waning antibody levels.

Despite multiple publications demonstrating differences in immune response between men and women,[28–32] we did not find a sex-based difference in our study. This may be due to a smaller cohort size (n=98) than most of the prior studies. It may also reflect the fact that we are studying immune responses nearly 20 years after multiple doses of MMR vaccine, as waning immunity and/or repeated immunization may obscure any sex-based immune response differences. Another limitation of the study is the time frame studied. Our investigation was limited by the existing biospecimens and available participants and therefore focused on a narrow window of time 7 and 17 years after vaccination. It is possible that a fair amount of waning had already occurred before we recruited subjects, and the extremely low cellular immune responses that we detected (especially to mumps) support this hypothesis.

While our study differs from the majority of published reports that demonstrated significant loss of mumps virus neutralizing antibody titers over time, it should be considered that, in the present study, we compared antibody titers in blood draws obtained ~17 years after vaccination to antibody titers in blood draws obtained ~7 years after vaccination. In contrast, most other studies made comparisons to serum obtained shortly after vaccination. It may be that vaccine-induced immunity wanes or drops relatively quickly in the early years after immunization and then stabilizes to a slower rate of decline at the timepoints available in our cohort (7-17 years post-vaccination). Nonetheless, not all studies have found clear evidence of loss of neutralizing antibody over time since vaccination. In a 2008 study by Date *et al.*, the geometric mean mumps virus neutralizing Ab titers in subjects vaccinated 1-5 years prior were higher (Geometric mean titer [GMT]=97, 95% CI: 64-148) than the titers in subjects vaccinated 16+ years prior (GMT= 58, 95% CI: 44-76), but this decrease was not significant (p=0.065) [8]. A 2009 study by LeBaron *et al.*, evaluated the persistence of mumps Ab after a second dose immunization with MMR. The authors found that titers rose slowly over the course of several years post-vaccination, but this was postulated to be due to exposure to wild type virus because a significant number of samples were obtained coincident with a nationwide increase in mumps cases [43]. Other factors may account for the difference between our results and those of others, including: 1) differences in cohort age/race/ethnicity, 2) variations in Ab testing methodology, and 3) small sample size of our cohort (n=98). In addition, while we limited our cohort to individuals who received only two doses of MMR, it is possible that some subjects had an undocumented, additional dose of vaccine, which could have boosted titers. Further, while we controlled for potential exposure as best we could (no known cases of measles or mumps have been documented in Olmsted County during the lifetimes of any subject), subjects may have traveled outside the county (for schooling, military service, or for work) during the intervening years between the first and second blood draws; therefore, it is possible that subclinical exposures may have occurred.

The changes observed in our cohort suggest that there is minimal waning of Ab titers between 7-17 years post-vaccination. This information, combined with the paucity of detectable cellular immune responses, suggests that most of the waning—if it occurs—has already happened by the timeframe we were able to study (i.e., 7-17 years post vaccination).

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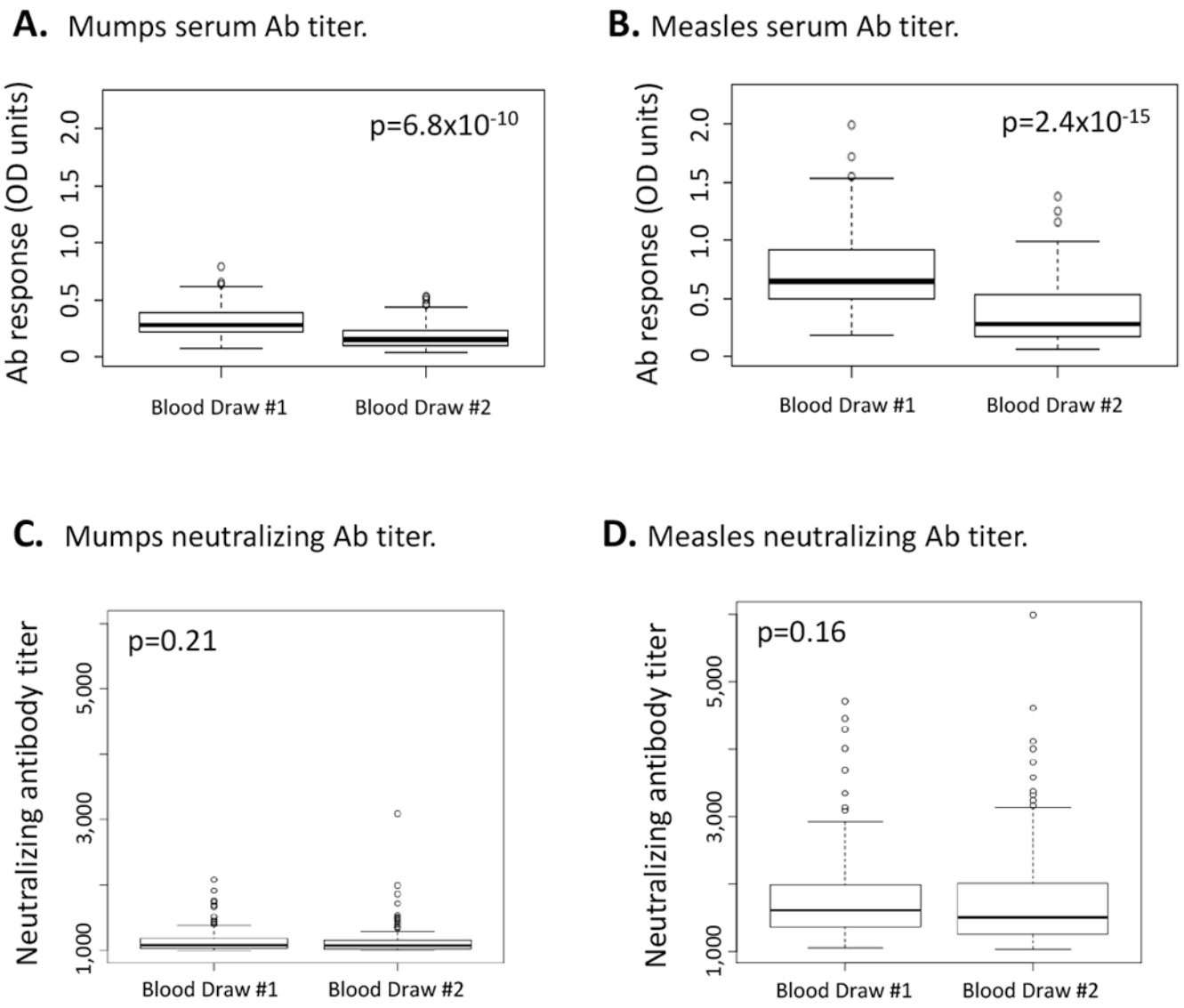

Figure 1. Measles and Mumps Serum IgG Titer and Neutralizing Ab Titer.

Virus-specific Ab titers (A and B) and neutralizing Ab titers (C and D) were measured as described in Methods. The box and whisker plots depict the median (solid line), interquartile range (boxes), and standard deviation (error bars), with the remaining data points plotted as open circles.

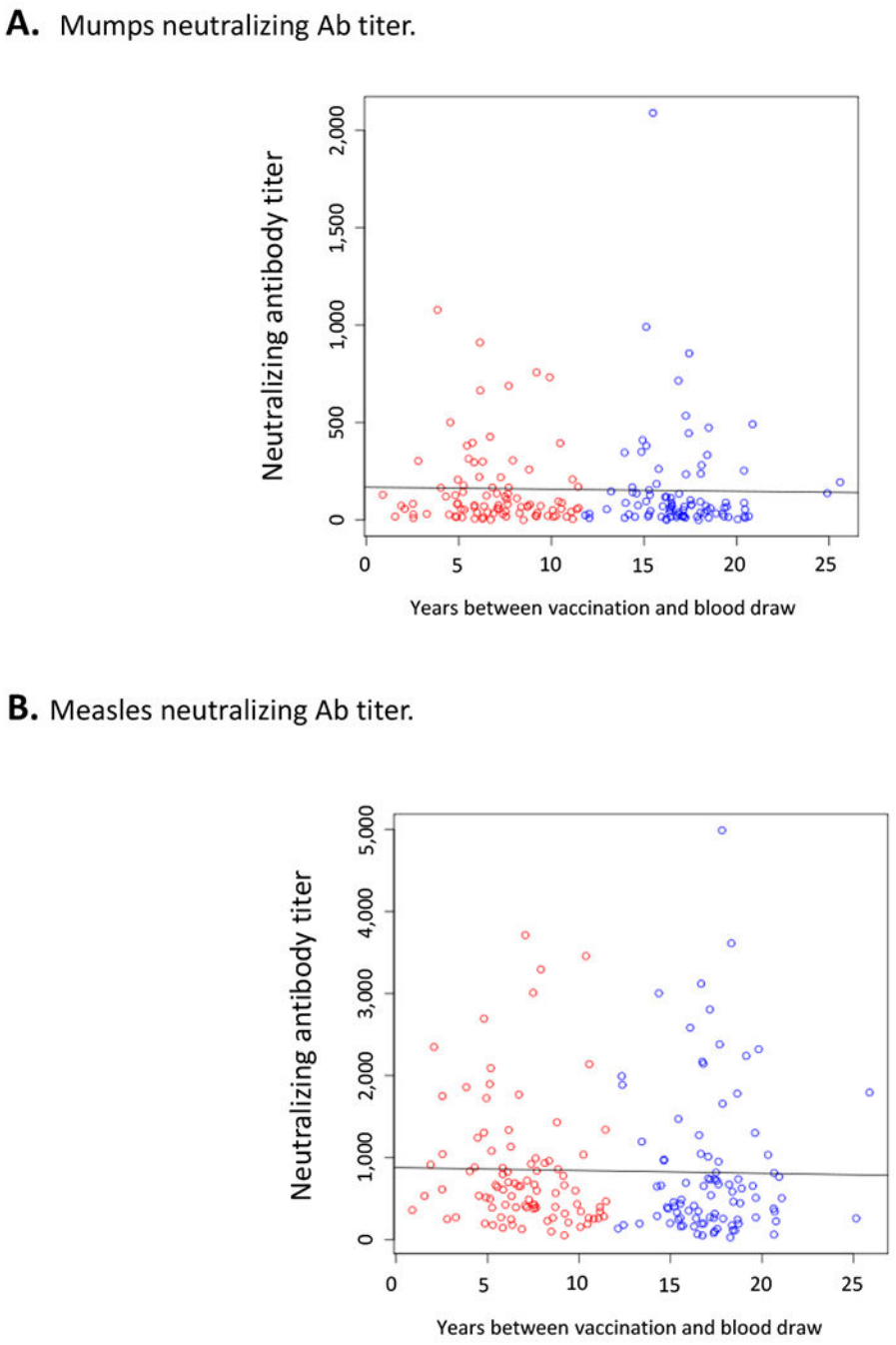

Figure 2. Effect of Time Since Vaccination on Neutralizing Antibody Response.

A) Mumps-specific neutralizing Ab titers were plotted as a function of time since last vaccination. B) Measles-specific neutralizing Ab titers were plotted as a function of time since last vaccination. Each subject underwent two blood draws (denoted by the red and blue circles). A linear regression line (black) was superimposed over the data.

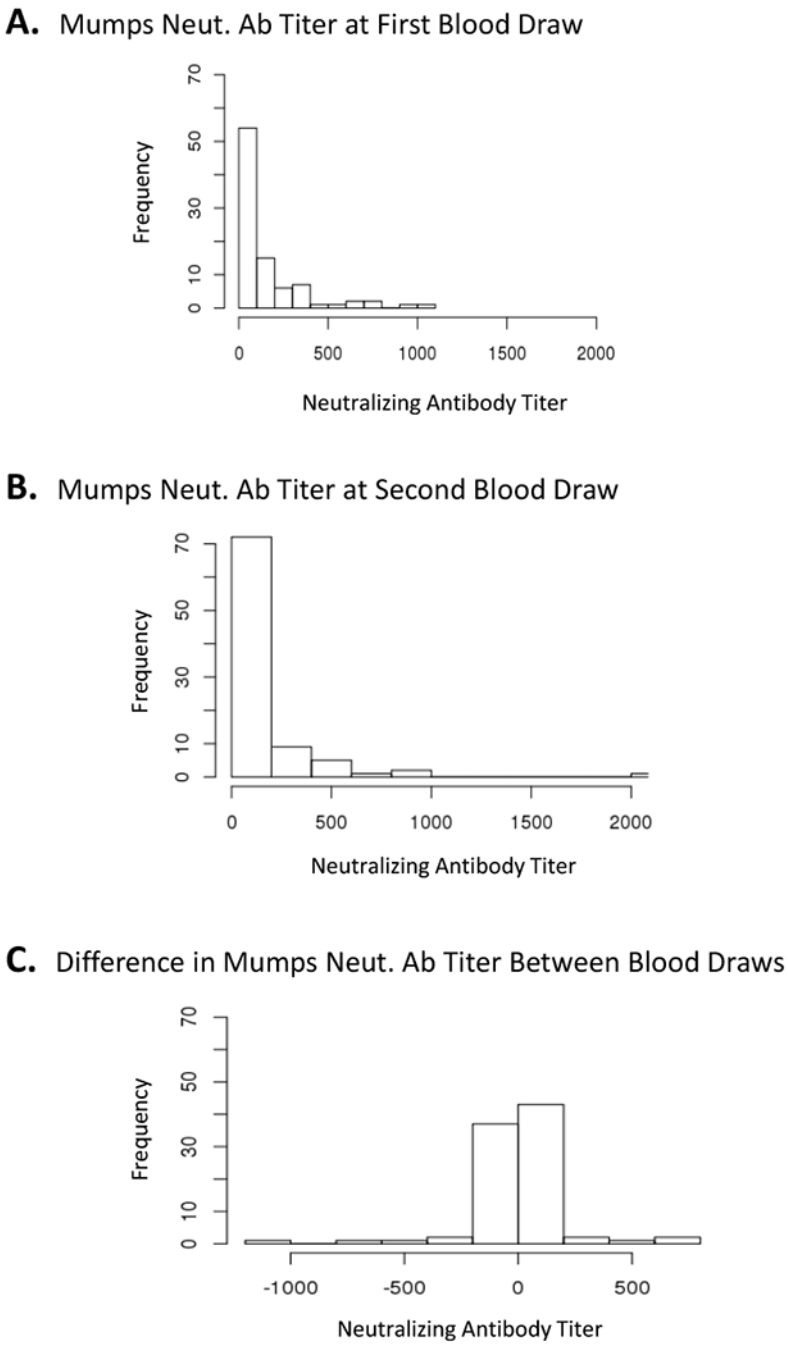

Figure 3. Mumps Neutralizing Antibody Titers At Each Blood Draw.

A) Mumps Ab titer at the initial blood draw ~8 years-postvaccination. B) Mumps Ab titer at the second blood draw ~15 years post-vaccination. C) Difference in titer between blood draws.

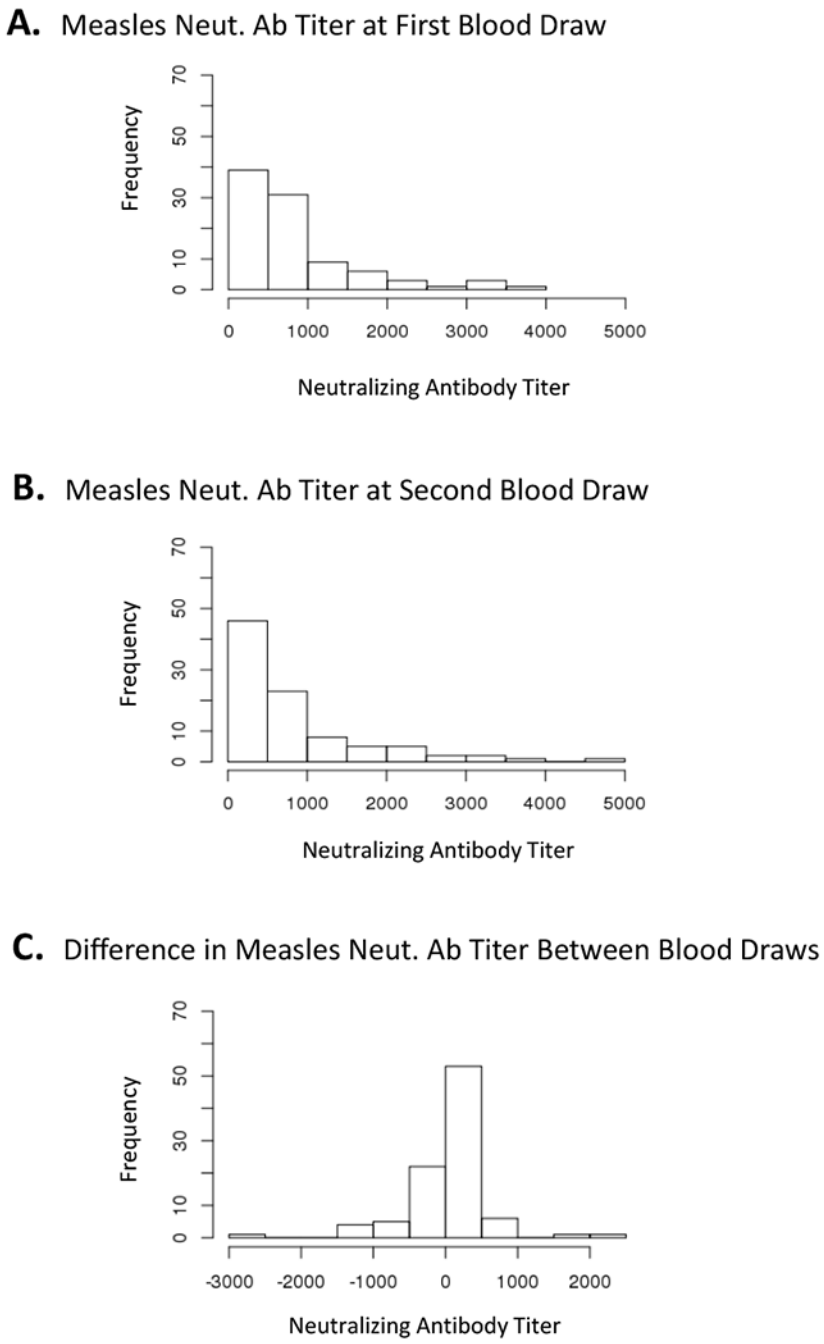

Figure 4. Measles Neutralizing Antibody Titers At Each Blood Draw.

A) Measles Ab titer at the initial blood draw ~8 years post-vaccination. B) Measles Ab titer at the second blood draw ~15 years post-vaccination. C) Difference in titer between blood draws.

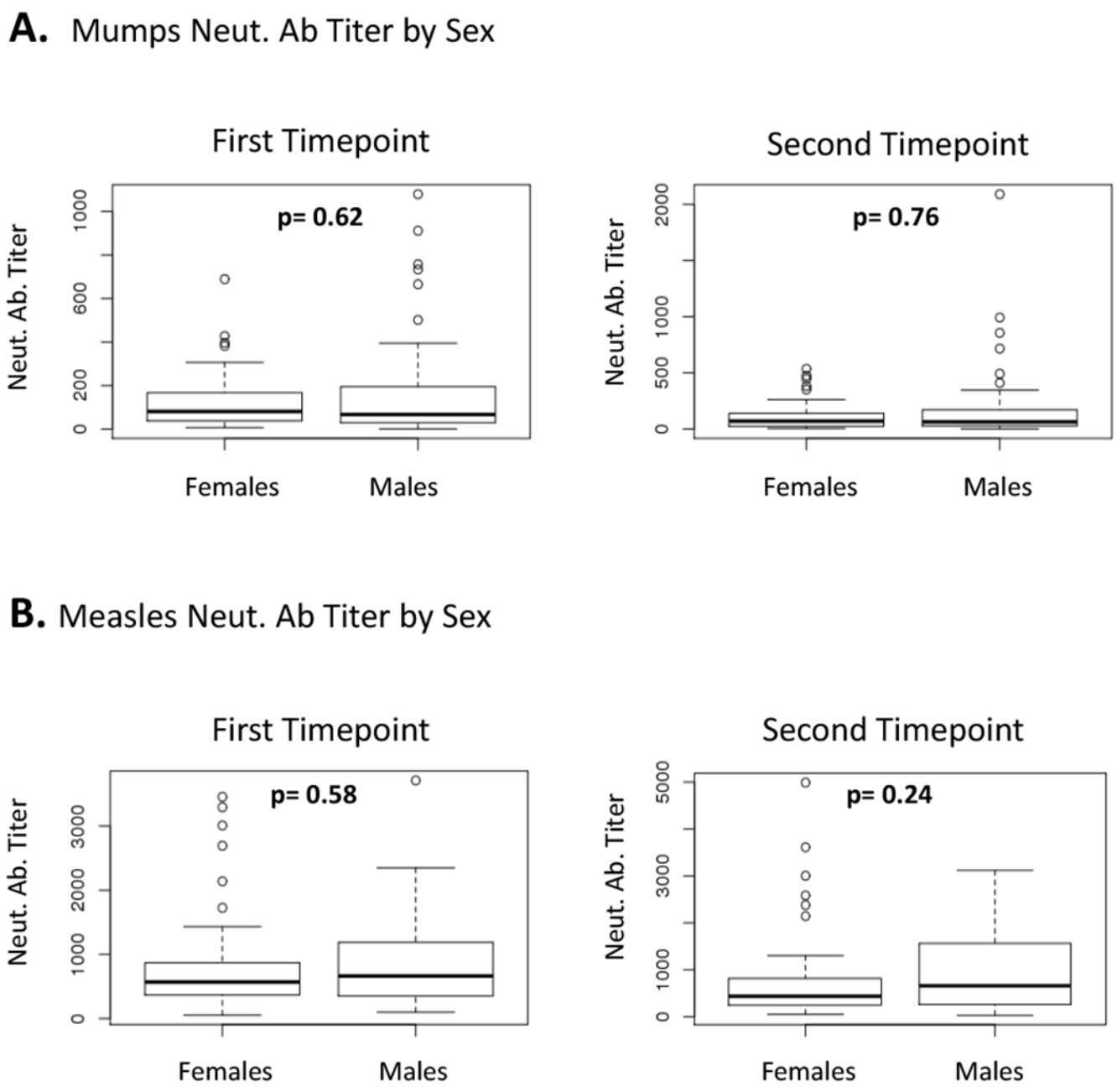

Figure 5. Sex Differences in Humoral Immune Response to Mumps and Measles.

A) Mumps neutralizing Ab titers in men and women. B) A) Measles neutralizing Ab titers in men and women.

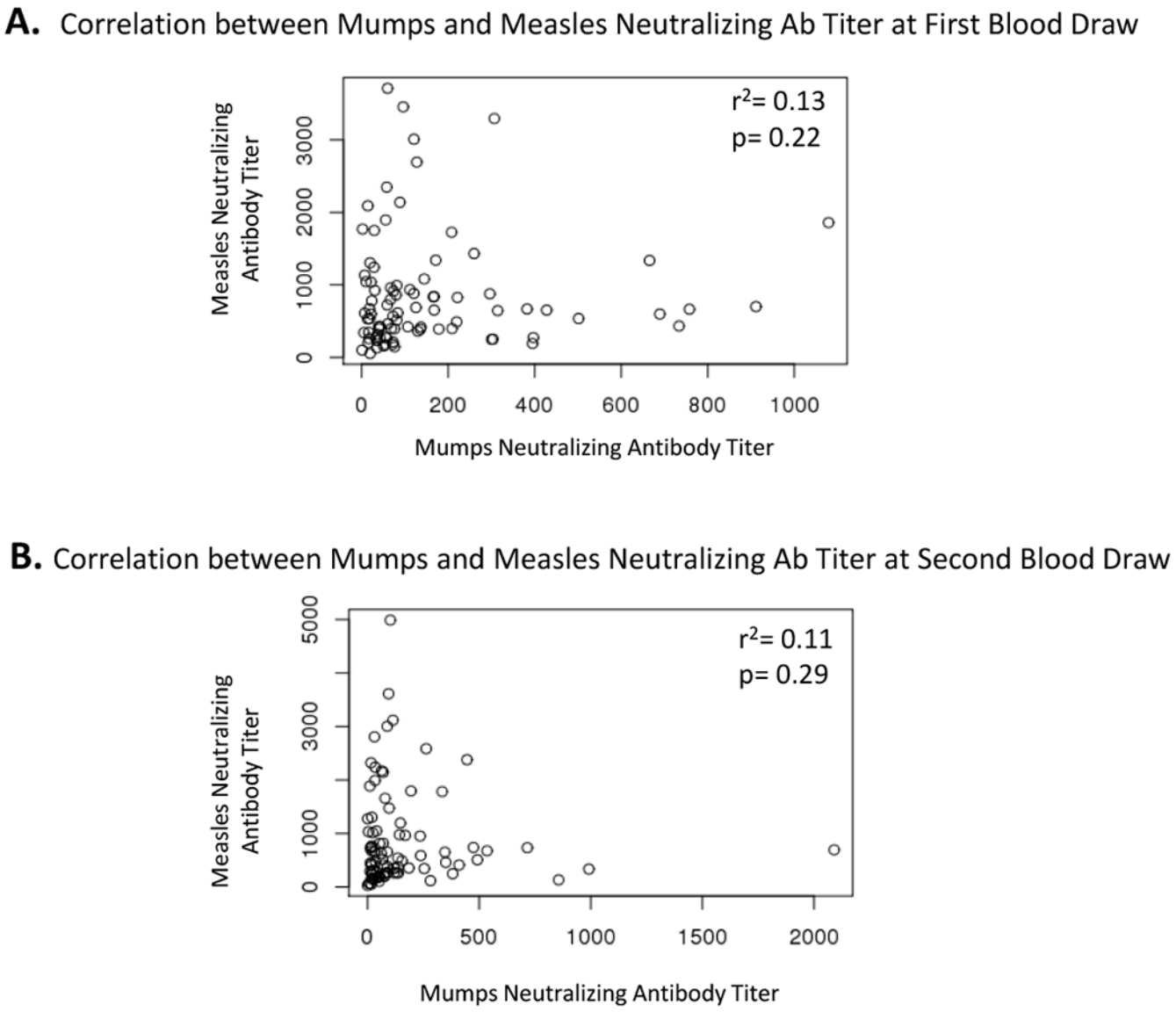

Figure 6. Correlation Between Mumps and Measles-Specific Immune Response.

A) Antibody titer correlation at first blood draw. B) Antibody titer correlation at second blood draw.

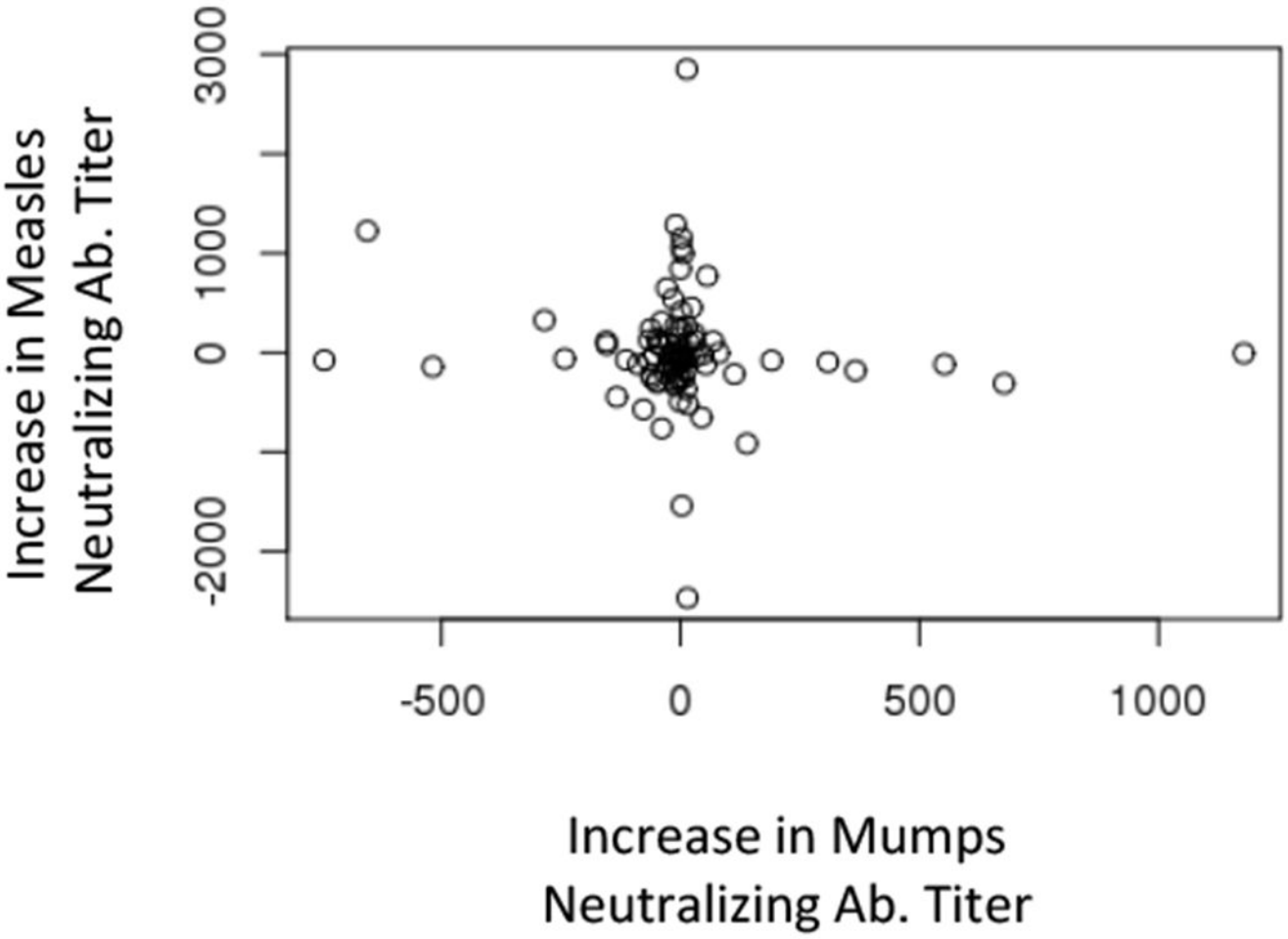

Figure 7. Comparison Between Change in Ab Titer Between Pathogens.

The change in measles neutralizing Ab titer (Y-axis) is compared to the change in mumps neutralizing Ab titer (X-axis). Each data point represents a single subject.

Table 1.

Study Cohort Demographics

Characteristic	
Cohort Size	98
Sex distribution	56.1% female 43.9% male
Race	1% Asian 99% Caucasian
Age at first blood draw	14 years old (IQR: 12.8 – 17)
Age at first vaccination	16.9 months old (IQR: 15 – 18)
Age at second vaccination	7 years old (IQR: 5–11)
Time since last vaccination at 1st blood draw	6.8 years (IQR: 5.2 – 8.7)
Time since last vaccination at 2nd blood draw	17 years (IQR: 15.3 – 18.4)
Time between blood draws	9.4 years (IQR: 7.6 – 14.2)